Application of Getts and Kadushin
Serial No. 10/050,088
Response of 9-22-2003 to Office Action of 3-20-2003

Remarks

Receipt is acknowledged of the Office Action dated March 20, 2003. Reconsideration of the application and a three month extension of the time provided for response are respectfully requested. The Commissioner is hereby authorized to debit all amounts due in this application from Deposit Account 50-1604.

In the Office Action, the Examiner rejected the claims of the application based on Hellyer et al. (U.S. Patent No. 6,207,818 B1), both individually and in combination with Lipshutz et al. (U.S. Patent No. 6,280,950 B1) and Kayyem (U.S. Patent No. 6,290,839 B1). Reconsideration of the rejections is respectfully requested.

The present invention is directed to a method for determining the presence of a specific nucleotide sequence in a target nucleic acid reagent. The method of the present invention involves concurrently contacting both a target nucleic acid reagent and a capture reagent to a microarray having a plurality of gene probes, followed by treatment of the microarray to induce the target nucleic acid reagent to hybridize with probes on the microarray and to induce the capture reagent to hybridize with the target nucleic acid reagent (the hybridizations being induced in either order). These two separate hybridization events are controlled using temperature, i.e. temperature is used while the target nucleic acid reagent and capture reagent are on the microarray to control which hybridization event will occur and when it will occur.

In other words, in accordance with the present invention, multiple components can be added together to the array for the purpose of conducting two separate types of hybridization. (The

components can be mixed together before application to the array, or they can be mixed on the array itself). Each desired hybridization process can then be "turned on" or "turned off" using temperature adjustments. Accordingly, in this method the components for multiple hybridizations can be added together to the array all at once, with kinetic considerations being used to control the different hybridization events, i.e. to "block" or reduce one type of hybridization from occurring, and to facilitate or enable another type of hybridization. This control is effected very elegantly by using temperature. As a result, a significant advance is provided in microarray assay procedures by significantly reducing the complexity of the procedure and the labor needed to conduct the assay.

Claim 1 has been amended to clarify that multiple temperatures are used to induce each of the two separate hybridization events, i.e. one temperature is used to facilitate the first hybridization and a second temperature is used to facilitate the second one. The claim has also been amended to clarify and improve its language, and to broaden it to indicate that the temperatures can be applied in either order (in other words, the user can start with either hybridization, as desired).

None of the references teaches or suggests this method, either individually or when taken in combination. Hellyer, for example, does not teach a method including two separate hybridization events wherein there is concurrent application of the components for the two hybridizations to the array, with the two separate hybridizations events on the array being regulated using different temperatures.

In Hellyer's Example 5 (the example cited against the claims of the Office Action), Hellyer teaches that "a flourescent labeled oligonucleotide (detector probe) is introduced in 6xSSC and allowed

to hybridize for 30 min at room temperature". *See,* Col. 20 lines 34-37. Thus, in Hellyer, once the flourescent labeled oligonucleotide is applied to the array, only one temperature is used for hybridization.

In contrast, as recited in step (a) of pending Claim 1, a microarray is concurrently contacted with both a target nucleic acid reagent and a capture reagent having label, followed by use of two different temperatures. One temperature is used to induce the target nucleic acid to hybridize to the complementary probe on the microarray, and another temperature is used to induce the capture reagent to hybridize to the capture sequence of the target nucleic acid. Hellyer does not teach or suggest this concurrent application of both a target reagent and capture reagent to a microarray, with two temperatures being used to control the two different hybridization events (the two different events being hybridization of target to probe, and hybridization of capture reagent to target).

Furthermore, as also recited in step (a) of Claim 1, the capture reagent of the present invention includes a first arm having a label capable of emitting a detectable signal and a second arm having a nucleotide sequence complementary to the capture sequence of the target molecule. Hellyer also does not teach or suggest such capture reagents.

Although the Office Action indicates that Hellyer's Example 5 teaches a capture reagent, Hellyer teaches addition of "capture probes" to a microelectronic array. The "capture probe" discussed in Hellyer, however, is just a molecule bound to a microelectronic array, i.e. it is merely a probe bound to an array. In contrast, in the present invention, a probe bound to an array (corresponding to what Hellyer calls a "capture probe") is hybridized to a target nucleic acid, and that target nucleic acid is

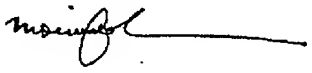
bound to what is referred to herein as a "capture reagent". That capture reagent has a first arm which binds to that target, and a second arm having a label. This does not appear to be taught or suggested in Hellyer in any manner.

In view of the above, it is submitted that the present invention is not anticipated by Hellyer, nor can it be obvious over Hellyer in conjunction with Lipshutz and/or Kayyem.

Accordingly, reconsideration of the rejections is respectfully requested. Favorable action on all of the claims and an allowance of the application is respectfully requested and believed fully warranted.

Dated: September 22, 2003

Respectfully submitted,



Morris E. Cohen (Reg. No. 39,947)
1122 Coney Island Avenue, Suite 217
Brooklyn, New York 11230
(718) 859-8009 (telephone)
(718) 859-3044 (facsimile)